

Formal Drawings:

The Office Action of July 18, 2000 and the current Office Action requested submission of formal drawings. Formal drawings are thus attached herein with this reply.

Nucleic Acid Sequence Listing:

The original application filed December 27, 1999 included a computer readable form and a printed form for the nucleic acid sequences referenced to in the present application, as well as a statement that the two sequence listings were identical. At the request of the Examiner, however, another copy of each is submitted with this response. Applicants respectfully submit that the requirements of 37 CFR §§ 1.821 through 1.825 have now been met.

In the Claims

Please amend claims 11, 57, and 64 to read as below, and add new claims 68 - 71.

In addition, please cancel claim 25 without prejudice.

11. (amended four times) A method for muting expression of an endogenous gene in a cultured population of animal cells, the method comprising the steps of:

(a) screening to identify [identifying] a muting nucleic acid composition having a sequence that is homologous to a sequence in the endogenous gene, the nucleic acid composition being double stranded[; and], wherein screening to identify comprises the steps

(i) engineering a set of DNA fragments encoding the endogenous gene into a plurality of vector molecules;

(ii) forming a plurality of transgenic cloned fragment recipients;

(iii) comparing expression of the endogenous gene in each of a subset of the cloned recipients to expression of the endogenous gene in the animal cells;

(b) delivering the muting nucleic acid into the population of cells; and

(c) muting expression of the endogenous gene at levels of transcription and post-transcription in the population as a whole, wherein such muting is independent of integration, expression, or transcription of the delivered nucleic acid.

57. (once amended) A method for muting expression of an endogenous gene in a cultured population of animal cells, the method comprising:

(a) [identifying] screening to identify a muting nucleic acid composition having a sequence that is homologous to a sequence in the endogenous gene, wherein the gene is one of a collagen, tumor necrosis factor (TNF), *tat*, and an immunoglobulin gene, the nucleic acid being double stranded~~;~~ and, wherein screening to identify comprises the steps

(i) engineering a set of DNA fragments encoding the endogenous gene into a plurality of vector molecules;

(ii) forming a plurality of transgenic cloned fragment recipients;

(iii) comparing expression of the endogenous gene in each of a subset of the cloned recipients to expression of the endogenous gene in the animal cells;

(b) delivering the muting nucleic acid into the population of cells; and

(c) muting expression of the endogenous gene at the levels of transcription and post-transcription in the population as a whole, wherein such muting is independent of integration, expression, or transcription of the delivered nucleic acid.

68. (new) A method for muting expression of an endogenous gene in a population of animal cells, the method comprising the steps of:

- (a) screening to identify a nucleic acid composition having a sequence that is homologous to a sequence in the endogenous gene, the nucleic acid composition being double stranded;
- (b) delivering the nucleic acid into the population of cells; and
- (c) muting expression of the endogenous gene at levels of transcription and post-transcription in the population as a whole, wherein such muting is independent of integration, expression, or transcription of the delivered nucleic acid.

69. (new) A method for muting expression of an endogenous gene in a population of animal cells, the method comprising:

- (a) screening to identify a nucleic acid composition having a sequence that is homologous to a sequence in the endogenous gene, wherein the gene is one of a collagen, tumor necrosis factor (TNF), *tat*, and an immunoglobulin gene, the nucleic acid being double stranded; and
- (b) delivering the nucleic acid into the population of cells; and
- (c) muting expression of the endogenous gene at the levels of transcription and post-transcription in the population as a whole, wherein such muting is independent of integration, expression, or transcription of the delivered nucleic acid.

70. (new) A method according to claim 68, wherein screening further comprises:

- (i) engineering a set of DNA fragments encoding the endogenous gene into a plurality of vector molecules;
- (ii) forming a plurality of transgenic cloned fragment recipients;